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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/847,010	05/01/2001	Perry A. Frey	032026-0476D	5359
23524	7590	08/23/2006		EXAMINER
FOLEY & LARDNER LLP				HUTSON, RICHARD G
150 EAST GILMAN STREET				
P.O. BOX 1497			ART UNIT	PAPER NUMBER
MADISON, WI 53701-1497				1652

DATE MAILED: 08/23/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	09/847,010	FREY ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Richard G. Hutson	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 05 June 2006.
- 2a) This action is FINAL.                    2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 29,37,40-48,59 and 60 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) Claim(s) 29,37 and 42-45 is/are allowed.
- 6) Claim(s) 40,41,46-48,59 and 60 is/are rejected.
- 7) Claim(s) \_\_\_\_\_ is/are objected to.
- 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
  - a) All    b) Some \* c) None of:
    1. Certified copies of the priority documents have been received.
    2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
    3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |   |  |
|---|--|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                    | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)              |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____. | 6) <input type="checkbox"/> Other: _____.  |

## DETAILED ACTION

Applicants cancellation of claims 30, 36, 38, 39, 52-58 and the amendment of claims 29, 40, 46 and the addition of claims 59 and 60, in the paper of 6/5/2006, are acknowledged. Claims 29, 37, 40-48, 59 and 60 are still at issue and are present for examination.

Applicants' arguments filed on 6/5/2006, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 40, 41, 46-48, 59 and 60 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 40, 41, 46-48, 59 and 60 are indefinite in that it is unclear as to what is encompassed by the referred to "conservative amino acid variant of SEQ ID NO: 4". It is unclear as to what activity or activities, if any the referred to "conservative amino acid variant of SEQ ID NO: 4" must maintain. Further, it is unclear as to what is encompassed by these claims with respect to "conservative amino acid variant of SEQ ID NO: 4" because it

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is unclear how many and what type of variants are encompassed by the referred to recitation.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 40, 41, 46-48, 59 and 60 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.\

Claims 40, 41, 46-48, 59 and 60 methods of producing L-β-lysine comprising the use of any conservative amino acid variant of SEQ ID NO: 4. The specification, however, only provides the representative species of methods of use of SEQ ID NO: 4, encompassed by these claims (See also above rejection under 112 second paragraph). There is no disclosure of any particular structure to function/activity relationship in the single disclosed species. The specification also fails to describe additional representative species of these conservative variants by any identifying structural characteristics or properties, for which no predictability of function is apparent.. Given this lack of additional representative species as encompassed by the claims, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and

exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at [www.uspto.gov](http://www.uspto.gov).

Claims 40, 41, 46-48, 59 and 60 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of producing L- $\beta$ -lysine comprising the use of the lysine 2,3-amino mutase having an amino acid sequence of SEQ ID NO: 4, does not reasonably provide enablement for any method of producing L- $\beta$ -lysine comprising the use of any lysine 2,3-amino mutase having an amino acid sequence having any conservative variant of SEQ ID NO: 4. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in *In re Wands* (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 40, 41, 46-48, 59 and 60 are so broad as to encompass any method of producing L- $\beta$ -lysine comprising the use of any lysine 2,3-amino mutase having an amino acid sequence having any conservative variant of SEQ ID NO: 4 (See also above 112 second paragraph rejection). The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of variants broadly encompassed by the claims, including any conservative amino acid variant of SEQ ID NO: 4. The claims rejected under this section of U.S.C. 112, first paragraph, minimal structural and no functional limits on the polypeptides used in the claimed methods. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to those methods of producing L- $\beta$ -lysine comprising the use of the lysine 2,3-amino mutase having an amino acid sequence of SEQ ID NO: 4.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is

unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all conservative modifications and fragments of SEQ ID NO: 4, because the specification does not establish: (A) regions of the protein structure which may be modified without effecting the desired activity; (B) the general tolerance of SEQ ID NO: 4 to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue of SEQ ID NO: 4 with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful. Because of this lack of guidance, the extended experimentation that would be required to determine which substitutions would be acceptable to retain the desired activity claimed and the fact that the relationship between the sequence of a peptide and its tertiary structure (i.e. its activity) are not well understood and are not predictable (e.g., see Ngo et al. in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495, Ref: U, Form-892), it would require undue experimentation for one skilled in the art to arrive at the majority of those polypeptides of the claimed genus having desired activity.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including those methods of use of conservative

amino acid modifications of SEQ ID NO: 4. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of those conservative variants having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

***Claim Rejections - 35 USC § 102***

The rejection of claims 30, 38 and 39 under 35 U.S.C. 102(b) as being anticipated by Chirpich et al. I (J. Biol. Chem. Vol. 245, No. 7, pp. 1778-1789, 1970, See IDS) is hereby withdrawn based on applicants amendment of 6/5/2006.

The rejection of claims 30, 38 and 39 under 35 U.S.C. 102(b) as being anticipated by Chirpich et al. (Preparative Biochemistry. Vol. 3, No. 1, pp. 47-52, 1973, See PTO-892, ref U) is hereby withdrawn based on applicants amendment of 6/5/2006.

***Claim Rejections - 35 USC § 103***

The rejection of claims 29, 37, 42, 43 and 45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chirpich et al. (J. Biol. Chem. Vol. 245, No. 7, pp. 1778-

1789, 1970, See IDS) is hereby withdrawn based on applicants amendment of 6/5/2006.

The rejection of claims 40 and 41 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Chirpich et al. (J. Biol. Chem. Vol. 245, No. 7, pp. 1778-1789, 1970, See IDS) as applied to claims 29, 37, 42, 43 and 45 above, further in view of Rozzell (U.S. Patent No. 4,88,0738), and Kusumoto et al. (Tetrahedron Letters, Vol 23, No. 29, pp 2961-2964) is hereby withdrawn based on applicants amendment of 6/5/2006.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G. Hutson whose telephone number is 571-272-0930. The examiner can normally be reached on M-F, 7:00-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Richard G Hutson, Ph.D.  
Primary Examiner  
Art Unit 1652

rgh  
1/30/2006